Remarks

Claims 21 and 23-34 are pending in this application. No claim amendments are made in this paper.[1] No new matter has been introduced.

Applicants respectfully submit that all of the pending claims are allowable for at least the following reasons.

A. The Rejection of Claims Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 2-4 of the Office Action, claims 21 and 23-28 are rejected as allegedly obvious over WO 92/00103 by Jones ("the '103 publication"), in view of U.S. Patent No. 5,712,302 to Young ("the '302 patent"). In particular, it is alleged that the claims are obvious because: 1) the '103 publication discloses a combination of 5-HT_3 antagonist and 5-HT reuptake inhibitor, and racemic ondansetron and fluoxetine are disclosed as a 5-HT_3 antagonist and a 5-HT reuptake inhibitor, respectively; and 2) the '302 patent discloses that R(+) ondansetron decreases adverse effects associated with racemic ondansetron. (Office Action, pages 3-4). Applicants respectfully disagree.

First, Applicants respectfully point out that while the '103 publication discloses ondansetron and fluoxetine, those of ordinary skill in the art would not have been motivated to specifically select these two agents and use them in a combination. This is because the combination of ondansetron and fluoxetine is merely one of numerous possible combinations disclosed in the '103 publication, and the '103 publication discloses nothing whatsoever regarding the desirability of that specific combination.

In response to Applicants' previous submission that at least four different combinations of three classes of molecules are disclosed in the '103 publication, the Examiner points to claim 2 of the '103 publication. (Office Action, page 4). The Examiner appears to suggest that since the combination of "5-HT_3 receptor antagonist and 5-HT re-uptake inhibitor" (one of the four different combination disclosed in the '103 publication) is claimed in the '103 publication, the '103 publication somehow provides a specific motivation for the combination of R(+) ondansetron and fluoxetine, as recited by claim 21. (*Id.*). Applicants respectfully disagree.

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[1] Applicants note that claims 29-34 are drawn to non-elected species. However, Applicants respectfully disagree with the Examiner's allegation that that there is "no allowable generic or linking claim." (Office Action, page 2). As discussed below, Applicants respectfully submit that claim 21, which is a claim linking claims 29-34, is allowable. For this reason, claims 29-34 are not deleted from the current application. Applicants will file a request for rejoinder at an appropriate time.

Applicants respectfully point out that claim 2, even if claiming one specific combination out of the four disclosed in the '103 publication, provides no more motivation or suggestion with regard to the combination it recites as compared to other combinations disclosed in the '103 publication. This is because the other three combinations disclosed in the '103 publication are all claimed in that reference as well. (*See* The '103 publication, claims 3, 4 and 5). Thus, it is clear that those skilled in the art, reading the '103 publication would be left with four different combinations of three different classes of compounds from which they should somehow select the specific combination of R(+) ondansetron[2] and fluoxetine. Considering that the '103 publication discloses numerous species for each of the classes it discloses, literally hundreds of different combinations are purportedly encompassed by the '103 publication. Yet, there is no teaching or suggestion in the '103 publication that the specific combination of ondansetron, much less optically pure R(+) ondansetron, and fluoxetine is particularly desirable.

Furthermore, the Examiner alleges, referring to col. 6, lines 1-29 of the '302 patent, that the '302 patent's disclosure that "clearer dose definition of efficacy vis a vis adverse effects may be achieved" by using R(+) ondansetron would have motivated those of ordinary skill in the art to replace the racemic ondansetron as disclosed in the '103 publication with R(+) ondansetron. Applicants respectfully disagree.

Applicants respectfully point out that those skilled in the art would not have been motivated to replace racemic ondansetron with R(+) ondansetron based on the teaching of the '103 publication and the '302 patent. First, as discussed above, those of ordinary skill in the art would not have been led to single out the combination of ondansetron and fluoxetine in the first place. Second, even assuming, *arguendo*, that those of ordinary skill in the art somehow arrived at the specific combination of racemic ondansetron and fluoxetine based on the disclosure of the '103 publication, the portions of the '302 patent referred to by the Examiner could not have motivated those skilled in the art to replace the racemic ondansetron with R(+) ondansetron. This is because while the '302 patent discloses, as the Examiner points out, that "clearer dose definitions of efficacy vis a vis adverse effects" may be achieved by using R(+) ondansetron, the '103 publication states, in connection with the combinations disclosed therein, that "no adverse toxicological effects are indicated with the

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[2] It should be noted that R(+) ondansetron is not even disclosed in the '103 publication. In addition, as discussed below, those skilled in the art would not have been motivated to replace racemic ondansetron, as disclosed in the '103 publication, with R(+) ondansetron, as disclosed in the '302 patent.

composition" disclosed therein. (The '103 publication, page 4, lines 10-12). Therefore, in view of this statement, those of ordinary skill in the art would not have been motivated to even look for a replacement for racemic ondansetron used in the combination disclosed in the '103 publication regardless of what the '302 patent discloses with regard to the adverse effects profiles of racemic and R(+) ondansetron.

For at least the foregoing reasons, Applicants respectfully submit that the pending claims are allowable, and thus request that the rejection under 35 U.S.C. § 103 be withdrawn.

No fee is believed due for this submission. However, if any fees are required for the entry of this paper or to avoid abandonment of this application, please charge the required fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

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